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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/648,304	08/25/2000	Airton Monza da Silveira	1369-00	6411

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PULLIAM, AMY E

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 11/20/2001

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/648,304	SILVEIRA ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Amy E Pulliam	1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 27 August 2001.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-23 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) \_\_\_\_\_ is/are rejected.
- 7) Claim(s) 1-23 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.
 

If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All
  - b) Some \*
  - c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
  - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s): _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

Receipt is acknowledged of the Corrected Filing Receipt, Amendment A, and the Priority Paper, received April 20, 2001, August 27, 2001, and September 13, 2001, respectively.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 2, 6-8, 12, 13, 21, and 22 remain rejected under 35 U.S.C. 102(e) as being anticipated by Ramtoola (US Patent 5,641,515). Ramtoola discloses a controlled release pharmaceutical formulation comprising nanoparticles formed of a biodegradable polycyanoacrylate polymer, wherein the active agent is complexed to the polycyanoacrylate. The disclosed particles are capable of releasing the active at a slower release rate than nanoparticles of free active agent (abstract). Ramtoola also teach that the size of the nanoparticles is between 50 and 900 nm (column 2, lines 57-58). Further, Ramtoola teaches that the nanoparticles have a drug loading of 15-25% (abstract).

***Response to Arguments***

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant argues that the cited reference does not anticipate the claimed invention because the reference does not teach each and every element of the claim. Applicant states that their invention includes nanoparticles which contain at least one active ingredient, and at least one compound capable of complexing the active ingredient, and a polymer, preferably polyalkylcyanoacrylate. Applicant states that the reference teaches a two-component system, as opposed to applicant's three component system. The examiner respectfully disagrees. As stated in the above rejection, Ramtoola teaches a pharmaceutical formulation comprising nanoparticles formed of a polycyanoacrylate polymer, where an active ingredient is complexed to the polymer. Although Ramtoola does not specifically teach a separate complexing agent in addition to the polymer, it is the position of the examiner that nothing in applicant's claim language prevents the polymer from acting as the complexing agent. Applicant's further argue that the complexing in Ramtoola is a result of a covalent bond formation between the active ingredient and the polymer, and that this method is distinct from the instant claims. Applicant additionally states that their invention involves the formation of non-covalent, low energy chemical bonds between the active ingredient and the complexing agent. However, applicant is discussing limitations which are not recited in the claim language. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988

F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, based on the very broad claim language of the above mentioned claims, this rejection is maintained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and 6-23 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ramtoola, as discussed above. Ramtoola is discussed as teachings a controlled release formulation of nanoparticles comprising a polycyanoacrylate polymer, and an active, wherein the active is complexed to the polymer. Ramtoola also teaches methods of making the nanoparticles, which suggest applicant's broad process claims. Furthermore, although Ramtoola does not teach the three specifically claimed active ingredients, it is the position of the examiner that applicant has placed no criticality on the specific drug, and therefore any drug could benefit from the controlled release formulation disclosed by Ramtoola. Absent any evidence of criticality, it is the position of the examiner that one of ordinary skill in the art would have been motivated to use any well known drug, which would benefit from controlled release properties, in the formulation disclosed by Ramtoola. The expected result would be a successful controlled release formulation. Therefore, this invention as a whole would have been

*prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

***Response to Arguments***

Applicant's arguments have been considered but are not found to be persuasive for the reasons stated above. Therefore, this rejection is maintained.

***Claim Rejections - 35 USC § 103***

Claims 1-5 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chen *et al.* (US Patent 5,932,248) and further in view of Trinh (US Patent 5,246,611). Chen *et al.* disclose a controlled release preparation comprising an ionic polymer matrix loaded with an active compound, wherein the active compound is a cytotoxic or cytostatic drug, and the active compound is complexed with a complexing agent in order to modify the release of the active from the polymer matrix (abstract). Chen *et al.* also teach doxorubicin as an exemplary active ingredient (column 14, claim 4). Chen *et al.* further teach that the ionic polymer matrix can be provided in the form of many types of formulations, including nanoparticles (column 3, lines 46-50). However, Chen *et al.* do not teach cyclodextrin as the complexing agent.

Trinh discloses cyclodextrin complexes. However, the disclosure of Trinh is relied upon for the teaching that cyclodextrin and its derivatives are very well known to act as complexing agents (column 1, lines 25-55). Furthermore, Trinh teaches that the teaching of cyclodextrins includes  $\alpha$ ,  $\beta$ , and gamma-cyclodextrins, and their derivatives, which are all known complexing agents.

Furthermore, it is the position of the examiner that one of ordinary skill in the art would have been motivated to use a different and known complexing agent in the formulation disclosed by Chen *et al.*, as Chen *et al.* disclose that this is acceptable, and especially because Trinh *et al.* teach that cyclodextrins are so well known as complexing agents. The expected result would be a successful microparticle or nanoparticle formulation with an active cytotoxic agent complexed by a complexing agent. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Response to Arguments***

Applicant's arguments have been considered but are not found to be persuasive. Applicant argues that by including a specific size for the nanoparticles into claim 1, the claims are no longer rendered obvious. The examiner respectfully disagrees. As stated in the above rejection, Chen *et al.* teach that their polymer matrix can be incorporated into many different types of formulations, including nanoparticles. It is the position of the examiner that specifying a particular range of nanoparticles does not render the claims patentable over the cited prior art, as this limitation would be routinely determined by one of ordinary skill in the art, through minimal experimentation, as being suitable, absent the presentation of some unusual and/ or unexpected results. The results must be those that accrue from the specific limitations. Therefore, this rejection is maintained.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is (703) 308-4710. The examiner can normally be reached on Mon-Thurs 7:30-5:00, alternate Fri 8:30-5:00.

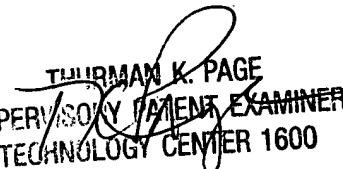
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 305-3592 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

aep

November 14, 2001

  
THIRMAN K. PAGE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600